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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER	
BOWERS, NATHAN ANDREW	
ART UNIT	**PAPER NUMBER**
1744	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/701,097	WEST ET AL.	
	Examiner	Art Unit	
	Nathan A. Bowers	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-114* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1-11, 55-64, 66, 68-77, and 111-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739).

With respect to claims 1 and 61-63, Mathies discloses a microfluidic chip comprising a plurality of flow channels (Figure 1:321, 323, 325, 327). Figure 8 depicts an embodiment of the invention wherein each channel contains a plurality of capture chambers (Figure 8:801, 803, 805, 807) that comprise microarrays for hybridization with biological analytes. This is disclosed in paragraphs [0073]-[0075]. Paragraph [0079] specifically teaches that the capture chambers contain nucleic acid probes immobilized within a viscous polymeric matrix. Paragraphs [0080]-[0082] state that other chambers may include a functionalized, porous, polymer monolith, and that antibody or nucleic acid probes may be immobilized upon the polymer monolith or the surface of the chambers in order to promote binding. The functionalized, porous, polymer monolith is highly crosslinked and comprises pores permitting fluid communication through the polymer monolith. In Figure 12 and paragraph [0091], Mathies teaches that the array chamber (Figure 12:1201) is surrounded by a plurality of vias (Figure 12:1211 and Figure 12:1213) through which fluids can be introduced and withdrawn. Mathies, however, discloses that the polymer monolith microarrays are used for the purification and isolation of biochemical analytes, and not for detection purposes. Accordingly, Mathies fails to teach the use of an observation port through which targets disposed within the microarray are capable of being detected.

McNeely discloses a microfluidic chip that utilizes a plurality of microarrays (Figure 27:154) as mean by which to detect various biochemical analytes in a sample solution. This is disclosed in paragraphs [0086]-[0088] and throughout the entire reference. Paragraph [0155] teaches that optical detection windows are further incorporated in the apparatus.

Mathies and McNeely are analogous art because they are from the same field of endeavor regarding microfabricated chips that comprise microarrays.

At the time of the invention, it would have been obvious to utilize the microarray disclosed by Mathies not only for purification purposes, but also for analyte detection purposes. Accordingly, it would have also been apparent to include an observation port in the apparatus disclosed by Mathies. McNeely teaches in paragraphs [0004]-[0008] that the use of microarrays to detect biochemical analytes is well known in the art, and that microarrays are effective in performing complex analyses of samples since they are capable of carrying out multiple detection reactions simultaneously. In the biomedical field, the use of microarrays for detection purposes is recognized as an effective way to diagnose various medical conditions, determine predisposition of patients to diseases, and perform DNA fingerprinting. Therefore, it would have been obvious to utilize an optical detection port in order to monitor target/ligand reactions in the capture chamber disclosed by Mathies. Since many hybridization systems involve fluorescence detection, the use of a transparent window is essential in order to determine and record binding.

It is believed that using microarrays for purification and using microarrays for detection are exceedingly similar acts. Both require selective binding of immobilized probes to analytes in a sample solution. Detection simply requires an additional step usually performed by an optical system. The selective binding of analytes to the microarray is identical in purification and detection procedures and therefore does not require any differences in the composition of the microarray probes.

With respect to claims 2-6, 8, 9, and 11, Mathies and McNeely disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Mathies teaches that the microarray comprises at least one probe, is capable of binding to a nucleic acid,

oligonucleotide, protein, antigen, or antibody target. Mathies discloses that nucleic acid probes are capable of hybridizing with nucleic acid targets. This is taught in paragraphs [0073]-[0082].

With respect to claims 7, 10, 59, 60, 76, and 77, Mathies and McNeely disclose the apparatus set forth in claims 5, 6, 56, and 75 as set forth in the 35 U.S.C. 103 rejection above. Although Mathies and McNeely do not expressly disclose the use of oligo-T and cDNA as probes and/or targets, it would have been obvious to do so. Both references teach that there are no restrictions to implementing essentially any type of biological polymer within the apparatus as long as it is capable of selectively binding. The references simply fail to expressly itemize cDNA and oligo-T. The use of oligo-T and cDNA as probes or as targets in hybridization reactions is well known in the art, and could have effectively been included in the apparatus disclosed by Mathies and McNeely.

With respect to claims 64 and 66, Mathies and McNeely disclose the apparatus set forth in claim 63 as set forth in the 35 U.S.C. 103 rejection above. Mathies teaches in paragraph [0083] that the functionalized, porous, polymer monolith is crosslinked with ethylene dimethacrylate, which serves to help immobilize probes on the pore surface.

With respect to claim 68, Mathies and McNeely disclose the apparatus set forth in claim 63 as set forth in the 35 U.S.C. 103 rejection above. Mathies teaches in paragraph [0080] that the polymer monolith comprises pores in the range of 10-20 microns. One of ordinary skill in the art would understand that pore ranges of 10-20 microns and those "smaller than about 10

microns" would perform identically during binding events. See *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

With respect to claims 69 and 70, Mathies and McNeely disclose the apparatus set forth in claim 63 as set forth in the 35 U.S.C. 103 rejection above. Although Mathies and McNeely do not expressly disclose void fractions and operating pressures, it would have been obvious to construct the polymer monolith to meet the claimed limitations. Varying the void fraction of the monolith to achieve the most favorable design is simply the optimization of result effective variables that could be pursued using routine experimentation. In the absence of new or unexpected results, it would have been obvious to ensure that the polymer monolith comprised a void fraction of less than 50% and was able to operate at pressures between 100 and 3,000 PSI. This would guarantee that the monolith would have had ample surface area to promote target binding, and would have been functional under pressure conditions that are typical of microarrays. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

With respect to claims 71-75, Mathies and McNeely disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Mathies teaches in paragraphs [0081]-[0083] that the functionalized porous polymer monolith comprises at least one functional group for binding a sample compound. Mathies states that azlactone, acrylate, and amide function groups may be linked to the porous monolith in order to promote binding to proteins, antibodies, and antigens. In paragraphs [0079] and [0086], Mathies discloses nucleic acid probes binding to nucleic acid targets. Although Mathies does not expressly disclose that

the functionalized polymer monolith is covalently bonded to the substrate, it would have been obvious to do so since it is beneficial and well known in the art to covalently bond probes and linker molecules to a support. Since the polymer monolith acts as a linker molecule by binding to the probes, and since the polymer monolith surface is easily functionalized, it would have been apparent to covalently bind the polymer monolith to the substrate.

With respect to claims 111-113, Mathies and McNeely disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. The capture chamber disclosed by Mathies containing the functionalized, porous, polymer monolith may intrinsically function as a derivatization reservoir that facilitates the trapping of target nucleic acids. Mathies discloses the use of protein ligands and protein receptors in paragraphs [0073]-[0079].

With respect to claim 114, Mathies and McNeely disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Mathies discloses the use of mobile, monolith valves capable of controlling fluid flow in paragraphs [0036]-[0044].

2) Claims 16-25, 31-44, and 51-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) as applied to claims 2 and 11, and further in view of Schembri (US 6875620).

With respect to claims 16-18, Mathies and McNeely disclose the apparatus set forth in claim 11 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that

the apparatus comprises a plurality of different probes that are capable of binding to different targets.

Schembri discloses a substrate (Figure 1:13) comprising a plurality of tiles (Figure 1:9) that contain immobilized probes upon their surfaces. In column 3, line 40 to column 4, line 40, Schembri states that an individual substrate may include a variety of different probes (Figure 1:11) that are each capable of binding to a unique target.

Mathies, McNeely, and Schembri are analogous art because they are from the same field of endeavor regarding the assembly of microarrays.

At the time of the invention, it would have been obvious to immobilize a variety of different probes within the apparatus disclosed by Mathies and McNeely in order to promote binding to a number of different targets. In column 2, lines 1-15, Schembri states that it is beneficial to incorporate probes comprising nucleic acids, proteins, polysaccharides, and lipids into the binding region with the intention of facilitating the simultaneous detection of a variety of analytes. In this way, the same device may be used to thoroughly evaluate a sample.

With respect to claims 19-25, 31-35, 43, 44, and 51-54, Mathies and McNeely disclose the apparatus set forth in claims 2 and 11 as set forth in the 35 U.S.C. 103 rejection above. In addition, McNeely seems to indicate in the Figures and in paragraphs [0086]-[0088] that the probes are disposed as spots fashioned in an ordered arrangement. However, this is not clearly disclosed in the specification.

Schembri discloses a microarray in which a plurality of probes (Figure 1:7) is arranged upon a plurality of tiles (Figure 1:9). The tiles function as "spots" that define affinity binding

regions. This is disclosed in column 3, line 40 to column 4, line 40. Column 3, lines 4-8 indicate that the tiles are between 40 and 250 microns wide. It is apparent from Figure 1 that the tiles are arranged in an orderly fashion and planarly arranged in two dimensions. Figure 2 discloses an embodiment in which the tiles are arranged in three dimensions. Column 3, lines 30-39 and column 4, lines 7-26 disclose that linker molecules (Figure 1:5) are used to covalently bind the probes to the device.

At the time of the invention, it would have been obvious to arrange the probes as spots upon the substrate of the apparatus disclosed by Mathies and McNeely. This would have been desirable because it would have defined distinct binding regions each comprising specific probes designed to capture specific targets. This would have provided an ordered and organized way to screen a sample solution for the presence of a plurality of certain analytes. Making the width of the spots 10 to 250 microns would have guaranteed that the spots were large enough to promote efficient detection, and small enough to allow the addition of many different spots.

Varying the sizes of the spots to achieve the most favorable design is simply the optimization of result effective variables that could be pursued using routine experimentation. In the absence of new or unexpected results, it would have been obvious to size the spots according to the claimed limitations. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

With respect to claims 36-42, Mathies, McNeely, and Schembri disclose the apparatus set forth in claim 35 as set forth in the 35 U.S.C. 103 rejection above. In addition, Mathies teaches that capture chambers (Figure 8:801, 803, 805, 807) are disposed within at least one microchannel (Figure 8:821). In light of the Schembri reference, these capture chambers would

contain a plurality of spots comprising a plurality of biological probes. From the Figure, it is clear that the microchannel comprises a rectangular serpentine path with first and second sections being separated by a wall. Although specific channel dimensions are not expressly disclosed, it would have been obvious to ensure that the width and length of the microchannel and sidewalls were adjusted to optimize hybridization and detection.

3) Claims 12-15, 19, 25-35, 43-46, and 48-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) as applied to claim 2 and 11, and further in view of Yamamoto (US 20040038388).

With respect to claims 12-15, 19, 25-35, 43-46 and 51-54, Mathies and McNeely disclose the apparatus set forth in claim 2 and 11 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the microarray comprises a plurality of neatly arranged spots, each containing up to about 50,000 probes and separated from each other by at least 100 microns and at most 500 microns.

Yamamoto discloses a substrate (Figure 4:410) comprising a plurality of probes arranged as a plurality of spots (Figure 4:420) across the substrate. Paragraph [0105] gives an example in which a spot contains 2,500 probes and another example in which a spot contains 48,400 probes. Probes are systematic arranged within the spots in rows and columns. For example, paragraph [0105] teaches that the spot containing 2,500 probes may be arranged as a square comprising 50 rows and 50 columns of probes. Paragraph [0090] states that the spots are physically separated by a distance with the range of 100 to 1,500 microns. Paragraph [0116] discloses an

embodiment in which the probes are disposed with microwells (Figure 4:440). Paragraph [0053] indicates that linker molecules are used to covalently bind the probes to the substrate.

At the time of the invention, it would have been obvious to immobilize a significant number of probes (1,000 to 50,000) at each spot within the apparatus disclosed by Mathies and McNeely. This would have ensured that the target analytes would have had ample opportunity to react with the array. It would have further been obvious to ensure that the spots were adequately spaced apart (100 to 1,500 microns) in order to clearly distinguish and locate binding events. Arranging the probes in a plurality of spots on the substrate would have been beneficial because it would have allowed one to group probes together in different arrangements in an effort to better analyze results. Varying the number of probes within the spots and the distances between spots to achieve the most favorable design is simply the optimization of result effective variables that could be pursued using routine experimentation. In the absence of new or unexpected results, it would have been obvious to construct the spots according to the claimed limitations. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

With respect to claims 48-50, Mathies and McNeely disclose the apparatus set forth in claim 2 and 11 as set forth in the 35 U.S.C. 103 rejection above. Although Mathies, McNeely, and Yamamoto do not expressly disclose that the plurality of probes comprise a disordered arrangement, it would have been obvious to construct the apparatus in this way. Randomly placing the plurality of probes requires less accuracy and precision during microarray construction, and therefore is likely to increase manufacturing speed and decrease cost. Unless an ordered arrangement is required by a specific application, randomly disposing probes across

the substrate would not decrease the likelihood of hybridization or the effectiveness of detection procedures.

4) Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) as applied to claim 64, and further in view of Klaerner (US 20020001845).

Mathies and McNeely disclose the apparatus set forth in claim 64 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose the use of glycidyl methacrylate.

Klaerner discloses a microarray device comprising a substrate covered by a polymer layer. The polymer layer is composed of a number of probes that are capable of binding to specific biological target molecules. Paragraphs [0126] and [0133] state that glycidyl methacrylate functional monomers are utilized in order to covalently attach probes to the polymer layer.

Mathies, McNeely, and Klaerner are analogous art because they are from the same field of endeavor regarding microarrays.

At the time of the invention, it would have been obvious to crosslink functionalized glycidyl methacrylate monomers to the porous polymer monolith disclosed by Mathies and McNeely. Klaerner teaches in paragraphs [0126] and [0133] that it is well known in the art to utilize glycidyl methacrylate as a means to covalently attach biological probes to a substrate. Since Mathies already teaches that a similar mono-ethylenically unsaturated monomer (ethylene dimethacrylate) is effective in binding certain probes to the surface of the polymer monolith, it

would have been obvious to incorporate similar monomer compounds, such as glycidyl methacrylate, to complete the same task.

5) Claims 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) as applied to claim 62, and further in view of Zare (US 20030062310).

Mathies and McNeely disclose the apparatus set forth in claim 63 as set forth in the 35 U.S.C. 103 rejection above. In addition, Mathies teaches in paragraphs [0081] and [0082] that UV light is used to catalyze polymer crosslinking. Mathies, however, does not expressly disclose the use of Irgacure 1800 during the UV activation.

Zare discloses a separation column which comprises a porous polymer matrix, and is used for the separation of biomolecules. Paragraphs [0069]-[0072] state that a photoinitiator is used to catalyze the polymerization of organic monomers to form the porous matrix. Paragraphs [0078]-[0081] specifically indicate that UV light and Irgacure 1800 are used during this catalytic step.

Mathies, McNeely, and Zare are analogous art because they are from the same field of endeavor regarding the use of photoinitiators to catalyze polymerization reactions in order to form a porous polymer matrix designed for the capture of biomolecules.

At the time of the invention, it would have been obvious to use UV light and Irgacure 1800 photoinitiators to aid in the formation of the functionalized porous polymer monolith. Zare teaches in paragraph [0080] that catalytic polymerization reactions involving Irgacure 1800 and UV are beneficial because they require a short preparation time, do not require high

temperatures, and produce a polymer product characterized by a high mechanical strength. Furthermore, this procedure is advantageous because it allows one to have control over what the pore sizes, placement, and length of the polymer product will be.

6) Claims 78-90, 93, 94, 96, 97, and 106-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) as applied to claim 1, and further in view of Werner (US 20020168652).

With respect to claims 78-83, 86-90, 93, 94, 96, 97, 106, and 107, Mathies and McNeely disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the microarray and the functionalized porous polymer monolith are disposed between a base substrate and a cover substrate.

Werner discloses microarray capture zones (Figure 3:148) that are disposed between a base substrate (Figure 3:146) and a cover (Figure 3:130). In Figures 8-11 and in paragraphs [0072]-[0075], Werner teaches that the microarray probes may be disposed on a top surface of the cover, or on the surface of the base substrate. In paragraphs [0096] and [0098], Werner discloses that the cover may be made clear in order to permit optical interrogation of the capture zones. A plurality of vias (Figure 3:132 and Figure 3:134) are disposed within the cover and are in fluid communication with the microarray. In paragraph [0082], Werner teaches that the vias are also capable of being in fluid communication with external fluidic devices (Figure 18:176) such as micropipettes carrying solutions to be analyzed. An adhesive layer (Figure 3:136) is used to bond the cover to the base substrate, and the microarray device comprises at least one microchannel (Figure 3:140) and reservoir (Figure 3:144).

Mathies, McNeely, and Werner are analogous art because they are from the same field of endeavor regarding the construction of microfluidic devices comprising biological probes.

At the time of the invention, it would have been obvious utilize a base substrate and a cover substrate in order to define a microfluidic system to contain the microarray and the functionalized porous polymer monolith disclosed by Mathies and McNeely. The use of these sandwich type arrangements is well known in the art, and is beneficial because sandwich arrays allow one to easily construct a system of microchannels and microwells between the cover and base. Furthermore, the fluidic system can be handled much easier and is less susceptible to contamination when the polymer monolith and the microarray are disposed between a cover and a base.

With respect claims 84 and 85, Mathies, McNeely, and Werner disclose the apparatus set forth in claim 86 as set forth in the 35 U.S.C. 103 rejection above. In addition, Werner teaches an arrangement in which a plurality of channels (Figure 3:142) are provided, each with its own set of microarrays (Figure 3:148) and vias (Figure 3:132). In this way, microarrays and vias are not in fluid communication with each other if they belong to separate channel structures. At the time of the invention, it would have been obvious to create a microarray system in which each of the individual hybridization areas were not fluidly connected. This would have been desirable if it was necessary to complete a plurality of separate screening procedures at once on a variety of different sample solutions.

With respect claims 108-110, Mathies, McNeely, and Werner disclose the apparatus set forth in claim 86 as set forth in the 35 U.S.C. 103 rejection above. In addition, McNeely teaches in paragraph [0155] that observation ports may constitute windows in the cover, and may be disposed across one or more channels and/or chambers of the device. At the time of the invention, it would have been obvious to ensure that the cover portion comprised at least one such observation port in order to allow visual inspection of the microarrays or polymer monoliths so that hybridization at specific probes may be detected.

7) Claims 91 and 98-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) and Werner (US 20020168652) as applied to claims 87 and 89, and further in view of Christel (US 6368871).

Mathies, McNeely, and Werner disclose the apparatus set forth in claims 87 and 89 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose specific microchannel dimensions, or that the apparatus further comprises microposts.

Christel discloses a sample chip comprising a body portion including a plurality of microchannels formed therein. Column 4, lines 1-2 state that the invention is designed for manipulating, controlling, and moving fluids on a microscale, and column 2, lines 7-12, Figures 1e-h, and Figure 2 teach that the microchannels are created in essentially any pattern or size. Christel teaches in column 6, lines 8-9 that these channels are typically 10-1,000 μm deep and 50 μm wide, and that fluids containing biological objects are introduced the channels via inlet and outlet ports, according to column 7, lines 57-64. The exact dimensions of the channel may be altered to meet the needs of specific applications. Column 7, lines 35-37 and column 11, lines

21-23 describe that a cover portion is bonded upon a body portion to effectively form a seal over the microchannels. Column 2, lines 46-55 and column 7, lines 10-20 describe that microchannels, as well as a number of microposts, are formed out of the chip by using a variety of etching, photolithography, and micromachining techniques. Column 2, lines 13-26 indicate that the microposts may selectively interact with and retain desired molecules, and column 8, lines 60 to column 9, line 7 teach that an electric field may be applied as an extra measure to hold molecules at the microposts. Individual microposts may be of any shape or size, according to column 7, lines 47-48, and are visually represented in Figures 1a-d. The microposts intrinsically may be fashioned at any sample chamber or at any point along the microchannels. The microposts may be utilized to enhance mixing.

Mathies, McNeely, Werner, and Christel are analogous art because they are from the same field of endeavor regarding microfluidic chips designed for the analysis of biological fluids.

At the time of the invention, it would have been obvious to incorporate a plurality of microposts into the apparatus disclosed by Mathies, McNeely, and Werner in order to enhance mixing of the fluid flowing through the microfluidic device. In column 4, lines 10-42, Christel teaches that mixing is a critical component of many biochemical analytical protocols, and can be enhanced by optimizing microchannel design and through the addition of microposts into the reaction area. Mixing is often difficult to achieve in microfluidic devices, and microposts offer an efficient alternative to more traditional macroscale methods. It would have further been obvious to ensure that the depth and width of the channels disclosed by Mathies, McNeely, and Werner were in the ranges of 10 to 100 microns and 100 to 10,000 microns, respectively.

Microfluidic devices comprising microchannels are desirable because they can carry out a thorough analysis using very small amounts of fluid, thereby reducing the costs associated with the purchase of reagents. It would have been obvious to optimize the depth and width of the channels carrying the biological targets to the microarrays for each specific procedure through routine experimentation.

8) Claims 92 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies (US 20040209354) in view of McNeely (US 20040037739) and Werner (US 20020168652) as applied to claims 90 and 93, and further in view of Regnier (US 6156273).

Mathies, McNeely, and Werner disclose the apparatus set forth in claims 90 and 93 as set forth in the 35 U.S.C. 103 rejection above. In addition, McNeely discloses an embodiment in which microarray reservoirs (Figure 19:194) are connected to a micromanifold (Figure 19:166). This is described in paragraphs [0098], [0099], [0116], and [0117]. McNeely, however, does not disclose that the micromanifold is in communication with a single chamber.

Regnier discloses a microfluidic system designed to separate analytes from a liquid stream. Regnier teaches that microfluidic channels (Figure 1:12) are periodically split in order to enhance the separation process and form a micromanifold (Figure 6:99). This is disclosed in column 3, line 36 to column 4, line 10 and column 11, lines 13-52.

Mathies, McNeely, Werner, and Regnier are analogous art because they are from the same field of endeavor regarding microfluidic biological systems.

At the time of the invention, it would have been obvious to utilize the micromanifold disclosed by Regnier at the reservoirs of the microarray disclosed by Mathies, McNeely, and

Werner. In column 12, lines 16-25, Regnier teaches that splitting a fluid channel into a plurality of individual offshoots is beneficial in microfluidic systems because it increases the contact area of the channel, which in turn allows one to more effectively capture and retain analytes in solution. This would have been desirable in the design of microarrays, since immobilized probes must come into physical contact with a desired target in order to detect its presence. Regnier further teaches that a micromanifold would have ensured that the linear velocity of the fluid and the pressure drop were constant at all points in the system. In this way, the incorporation of a micromanifold into the device proposed by Mathies, McNeely, and Werner prior to the reservoir and microarray would have advantageously equalized the pressure distribution within the structure.

Response to Arguments

Applicant's arguments, see pages 4-15, filed 26 June 2006, with respect to the rejection(s) of claim(s) 1-11, 55-64, 66, 68-77 and 111-114 involving Mathies in view of Alajoki under 35 U.S.C. 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the combination of Mathies and McNeely.

It is believed that the deficiencies of Mathies are addressed by McNeely. The McNeely reference is superior to the Alajoki reference in that it clearly discloses a microfluidic chip comprising a plurality of microarrays in communication with an observation port. As described in the 35 U.S.C. 103 rejection above, McNeely gives motivation that would persuade one of ordinary skill in the art to utilize the functionalized porous polymer monolith microarray in the

detection of analytes, rather than simply just in their purification. Consequently, it would have additionally been obvious to include an observation port capable of facilitating optical detection.

It is believed that using microarrays for purification and using microarrays for detection are exceedingly similar acts. Both require selective binding of immobilized probes to analytes in a sample solution. Detection simply requires an additional step usually performed by an optical system. The selective binding of analytes to the microarray is identical in purification and detection procedures and therefore does not require any differences in the composition of the microarray probes.

Conclusion

This is a non-final rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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NAB

GLADYS JP CORCORAN
SUPERVISORY PATENT EXAMINER